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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/562,059

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Yasuhiro Kajihara

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KUBOVCIK & KUBOVCIK

SUITE 1105

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EXAMINER

OLSON, ERIC

ART UNIT

PAPER NUMBER

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/562,059	<b>Applicant(s)</b> KAJIHARA ET AL.	
	<b>Examiner</b> Eric S. Olson	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2-8, 12, 13, 15 and 16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-8, 12, 13, 15 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **Detailed Action**

This office action is a response to applicant's communication submitted June 23, 2008 wherein claims 2, 5, 7, and 8 are amended and claims 1, 9-11, 14, and 17-20 are cancelled. This application is a national stage application of PCT/JP04/09521, filed June 29, 2004, which claims priority to foreign application JP2003-187931, filed June 30, 2003.

Claims 2-8, 12,13, 15, and 16 are pending in this application.

Claims 2-8, 12,13, 15, and 16 as amended are examined on the merits herein.

Applicant's amendment, submitted June 23, 2008, with respect to the objection to claims 17-20 for improper grammar, has been fully considered and found to be persuasive to remove the objection. Therefore the objection is withdrawn.

Applicant's amendment, submitted June 23, 2008, with respect to the rejection of instant claims 9, 10, and 17-20 under 25 USC 112, first paragraph, for lacking enablement for methods of preventing or curing influenza viral infection, has been fully considered and found to be persuasive to remove the rejection as the rejected claims have been cancelled. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-8, 12,13, 15, and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific asparagine-linked disialoundecaoligosaccharide-fatty acid amides disclosed in the specification, does not reasonably provide enablement for any asparagine-linked disialoundecaoligosaccharide-fatty acid amide whatsoever. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a chemical compound comprising a disialo-oligosaccharide linked to asparagine linked to a fatty acid. In order for a compound to be enabled by the specification, the specification must enable one skilled in the art to use the compound for some purpose.

The state of the prior art: Certain glycoproteins can be degraded to produce asparagine-linked oligosaccharides containing sialic acid, for example Lowe et al. and Endo et al., both of which are included with Applicant's form PTO-1449. However, these compounds and their fatty acid derivatives are not known in the art to be useful for any purpose, for example as therapeutic agents.

The relative skill of those in the art: The relative skill in the art is high.

The predictability or unpredictability of the art: There exist many different sialyl-containing polysaccharides *in vivo* and many molecular receptors or other proteins that recognize them. The diversity of possible carbohydrate structures leads to a vast diversity of different biological effects. Therefore for any novel carbohydrate, it is highly unpredictable what effect it will produce *in vivo* or what possible biological or medical use, if any, it might have. Therefore the subject matter of the claimed invention is highly complex.

The Breadth of the claims: The claimed invention includes any molecule whatsoever that includes an oligosaccharide of 11 units, straight or branched, containing two sialic acid units, with the oligosaccharide linked to an asparagine molecule which is linked to a fatty acid by an amide bond. Therefore an enormous diversity of different carbohydrate structures are included in the claimed invention.

The amount of direction or guidance presented: Applicant's specification discloses that certain specific asparagine-linked disialoundecaoligosaccharide-fatty acid amides inhibit influenza sialidase, and are thus potentially useful for the treatment of

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influenza. This activity is not shown to be present in any significant fraction of the vast diversity of carbohydrates included within the scope of the claimed invention.

The presence or absence of working examples: no working examples are shown for any practical use of the claimed invention, for example treatment of influenza.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the biological role of complex oligosaccharides. See MPEP 2164.

The quantity of experimentation necessary: In order to actually use the vast majority of oligosaccharides falling within the scope of the claimed invention, one skilled in the art would have to determine what the various oligosaccharides can actually be used for. Applicant's specification only provides one possible use for a narrow group of these compounds. One skilled in the art would thus have to undertake a large-scale program of research in order to discover novel uses for many novel compounds, And to determine which of these compounds are or are not useful for anything in the first place. Doing so would involve an undue burden of unpredictable experimentation.

*Genentech*, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the unpredictability of the art, Applicants fail to provide

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information sufficient to practice the claimed invention for all possible asparagine-linked disialoundecaoligosaccharide-fatty acid amides.

Response to Argument: Applicant's arguments, submitted June 23, 2008, has been fully considered as it relates to the above ground of rejection and not found to be persuasive to remove the rejection. Applicant argues that the most recent amendment overcomes this rejection by specifying a particular length for the fatty acid chain. However, as explained above, the rejection is based on the wide number of **oligosaccharides** that are included in the scope of the claims. This issue has not been addressed. Although one skilled in the art would be able to make and test some oligosaccharide structures, the vast number of oligosaccharides claimed would include such a diversity of different molecules that making and evaluating all of them would involve an undue burden of unpredictable experimentation.

Therefore the rejection is deemed proper and made **FINAL**.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-5, 7, 8, 12, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Michel et al. (Reference included with PTO-892) Michel et al. discloses a coupling of sialoglycopeptides to fatty acids. (p. 2365, first paragraph of introduction, p.

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2366 under the heading *Coupling Reaction*) A glycopeptide comprising a biantennary disialo-undecaoligosaccharide linked to asparagine was isolated and coupled to palmitic acid, which is a 16-carbon straight-chain saturated fatty acid. (p. 2367, under the headings *Glycopeptide Isolation* and *Coupling*) This conjugate is an asparagine-linked disialoundecaoligosaccharide according to the instant claims, and is reasonably considered to have the utility disclosed in the instant claims for treating influenza. Furthermore, it is dissolved in DMSO, which is reasonably considered to be a pharmaceutical additive. (p. 2367, bottom of page) Therefore the claimed invention is anticipated by Michel et al.

Response to Argument: Applicant's arguments, submitted June 23, 2008, has been fully considered as it relates to the above ground of rejection and not found to be persuasive to remove the rejection. Applicant argues that the claimed conjugate contains only an asparagine amino acid connected to the glycan, while the prior art compounds include dipeptides and larger peptides containing multiple amino acids. However, this limitation is not recited in the claims. The claims only require that the conjugate be asparagine-linked, which is interpreted as meaning that at least one of the glycan or the fatty acid be linked to asparagine. Therefore the claims include the prior art compounds of Michel et al. Furthermore, the amino acid ratio disclosed by Michel et al. includes 1 mole of asparagine to 0.75 mol of other amino acids. This means that about 25% of the conjugate molecules are asparagine mono-aminoacid conjugates. Therefore the composition described by Michel et al. does include conjugates linked by asparagine alone.



For these reasons the rejection is deemed proper and made **FINAL**.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 6 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Michel et al. (Reference included with PTO-892) in view of Remington: The Science and Practice of Pharmacy, Twentieth Edition. (Reference included with PTO-892, herein referred to as Remington) The disclosure of Michel et al. is discussed above. Michel et al. does not disclose a composition further comprising any of the additives recited in instant claims 6 and 14-16.

Remington discloses glycerin as a pharmaceutical solvent, (p. 735, left column paragraph 4) and lactose, mannitol, glucose, and sucrose as diluents or binders for pharmaceutical tablets. (p. 860, left column last paragraph, right column paragraph 4)

It would have been obvious to one of ordinary skill in the art at the time of the invention to add any of the additives disclosed by Remington to the compounds discussed by Michel et al. These additives are well known in the art, and one of ordinary skill in the art would have realized that they could be productively used as a binder, diluent, or solvent for a prior art active agent.

Thus the invention taken as a whole is *prima facie* obvious.

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Response to Argument: Applicant's arguments, submitted June 23, 2008, has been fully considered as it relates to the above ground of rejection and not found to be persuasive to remove the rejection. Applicant argues that the claimed conjugate contains only an asparagine amino acid connected to the glycan, while the prior art compounds include dipeptides and larger peptides containing multiple amino acids. However, this limitation is not recited in the claims. The claims only require that the conjugate be asparagine-linked, which is interpreted as meaning that at least one of the glycan or the fatty acid be linked to asparagine. Therefore the claims include the prior art compounds of Michel et al. Furthermore, the amino acid ratio disclosed by Michel et al. includes 1 mole of asparagine to 0.75 mol of other amino acids. This means that about 25% of the conjugate molecules are asparagine mono-aminoacid conjugates. Therefore the composition described by Michel et al. does include conjugates linked by asparagine alone.

For these reasons the rejection is deemed proper and made **FINAL**.

### **Conclusion**

No claims are allowed in this application. **THIS ACTION IS MADE FINAL.**

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/  
Examiner, Art Unit 1623  
9/3/2008

/Shaojia Anna Jiang, Ph.D./  
Supervisory Patent Examiner, Art Unit 1623